apical region at cell division acquire polarity, adopt an outside position and become trophectoderm, whereas those that do not inherit an apical region are internalized and become ICM.

The molecular mechanisms that link cell polarity to the first cell-fate choices remained a mystery for many years. But recently, differential activity of the Hippo signalling pathway was shown to be crucial for the decision[8]. Despite this advance, exactly how position and polarity cues translate into differences in Hippo pathway activity remained unclear. Adding to this disparate body of knowledge, accumulating evidence[9,10] indicated that a cell's position depends on its contractility. Maitre and colleagues' study[1] combines theory and experiment to unify the existing models of ICM–trophectoderm fate choice, and also provides a mechanistic link between cell polarity, position and Hippo pathway activity (Fig. 1).

The authors showed that asymmetric segregation of a polarized apical domain at cell division generates two daughter blastomeres with differential levels of contractility. Daughter cells that receive the apical domain are less contractile than their apolar sisters. The researchers then found that apolar blastomeres have higher levels of the scaffolding protein actomyosin than their polarized counterparts, directly translating into increased contractility. These differences in contractility trigger the sorting of cells to internal or external positions, because the less-contractile polarized cells have a tendency to spread over the apolar cells, which become internalized.

Support for this model came from a series of experiments in which Maitre *et al.* measured the surface tension of individual blastomeres, and then traced those cells over time in embryos to determine which lineage they adopted. This involved the development of technically sophisticated methods to probe the mechanics of individual cells and then track cells in embryos. Furthermore, the authors found that altering a cell's contractility altered its fate.

Finally, they demonstrated that contractility controls the subcellular position of the transcriptional co-activator protein Yap, a central component of the Hippo pathway. In less-contractile, polarized cells, Yap translocated to the nucleus, leading to activation of trophectoderm-specific genes. In apolar, highly contractile cells, Yap remained excluded from the nucleus. Linking Yap activity to differences in cell contractility connects the mechanical properties of blastomeres to their cell-fate choices, suggesting that mechanosensing may affect early lineage decisions.

Mammalian embryos are renowned for their ability to develop normally following alterations in internal architecture, or the loss or addition of cells. It has been proposed[11] that activation of dormant mechanisms might help embryos to successfully carry out development following perturbations. Indeed, Maitre *et al.* showed that the mechanism responsible for ICM or trophectoderm specification is also probably used to compensate for perturbations, and thus underpins the regulative nature of mammalian embryos. By mixing cells with differential contractility, the authors demonstrated that those with elevated contractility adopted an internal position within embryos, whereas those with reduced contractility adopted an outside position. A mechanistic link between the position of a cell, its contractility and its gene-expression profile explains how the cell might 'sense' and consequently 'adjust' its position in the embryo, altering gene expression accordingly.

Although the current study represents a major breakthrough in our understanding of early mammalian development, several questions remain open. For instance, it is still not clear what triggers the initial blastomere polarization and differential contractility. It has been shown that modulating key transcription factors that control cell fate can influence cell position within an embryo, and so a feedback mechanism perhaps translates changes in gene expression into changes in contractility. In addition, the mechanism by which actomyosin affects the subcellular positioning of Yap needs to be determined.

Perhaps most important is that the results of Maitre and colleagues' study beg the question of whether the same mechanism is used in a variety of developmental contexts. Is mechanosensing through cellular contractility repeatedly used to regulate a cell's propensity to adopt alternative fates? The answer is sure to provide valuable insights into how lineage decisions are made in the mammalian embryo. ■

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CONDENSED-MATTER PHYSICS

Superconducting electrons go missing

'Overdoped' high-temperature superconductors, which have a high density of charge carriers, were thought to be well understood. An experiment challenges what we know about quantum physics in such systems. SEE LETTER P.309

JAN ZAANEN

Put a large number of interacting quantum particles together and exotic things can happen. A landmark example is superconductivity[1], in which certain materials have zero electrical resistance when cooled below a critical temperature, T_c. The first such materials to be discovered were superconductive only at low temperatures (T_c of a few kelvin), and their behaviour could be explained by the Bardeen–Cooper–Schrieffer (BCS) theory[2]. Superconductivity was considered a closed chapter until the surprising discovery in 1986 of high-temperature copper oxide superconductors[3] (T_c of up to 160 K), whose properties couldn't be described by BCS theory[4]. Nevertheless, it was thought that overdoping such superconductors — significantly increasing the density of charge carriers and thereby reducing the materials' T_c — would bring them into agreement with the theory[4]. Božović *et al.*[5] show on page 309 that even this overdoped regime is highly anomalous, a finding that has implications for our fundamental understanding of superconductivity.

In quantum statistics, particles called bosons can exist in the same quantum state, whereas fermion particles must occupy different states — a restriction called the Pauli exclusion principle. If many bosons occupy the lowest energy state of a system (a configuration known

as a Bose condensate), the microscopic quantum behaviour gets amplified to the macroscopic scale, and the result is superconductivity.

BCS theory explains how electrons can form a Bose condensate, even though they are fermions. The natural state of fermions is as a Fermi gas, in which the particles fill up the lowest energy levels of a system, according to the Pauli exclusion principle. The boundary between the filled and unfilled energy levels is known as the Fermi surface. In BCS theory, upon introducing a small attractive interaction between the electrons in a system, those electrons closest to the Fermi surface bind together to form what are called Cooper pairs[1,2]. Because these Cooper pairs are effectively bosons, they form a Bose condensate.

One might expect that only the small fraction of electrons that form Cooper pairs contributes to superconductivity, but in fact all the electrons in the Fermi gas participate. The density of superconductive electrons (the superfluid density) is therefore approximately equal to the total electron density — a prediction that has been confirmed experimentally in many 'conventional' superconductors[1].

The situation is less straightforward for copper oxide superconductors because the electrons in these systems interact strongly[4]. The electrons behave like cars on a motorway[6], forming a traffic jam (a 'Mott insulator'[7]) when the density is high. Doping the system is equivalent to reducing the density of cars on the motorway, which gives rise to a kind of stop–start traffic. The result is that T_c increases with doping, reaching a maximum at a level known as optimal doping.

In the overdoped regime (when doping has increased beyond optimal doping), the cars (electrons) move more freely and no longer interact strongly, leading to a reduction in T_c. In this weakly interacting regime, one might expect the system to be described by BCS theory[4]. This expectation seemed to be confirmed when a Fermi surface subjected to textbook Cooper pairing was directly observed in a variety of overdoped systems[8,9]. Because, in BCS theory, the superfluid density is approximately equal to the total electron density, it should be large and almost independent of both doping and T_c.

Božović and colleagues present the first reliable measurements of the superfluid density in the overdoped regime. Such measurements have taken so long to obtain because the material is difficult to prepare: overdoped copper oxides are chemically unstable. But, in an impressive feat of materials engineering, the authors manage to prepare near-perfect samples using sophisticated techniques.

By measuring the superfluid density as a function of doping, the authors find that there are far fewer superconducting electrons than expected from BCS theory (Fig. 1a) — most of these electrons seem to be missing. The authors also demonstrate a simple scaling law

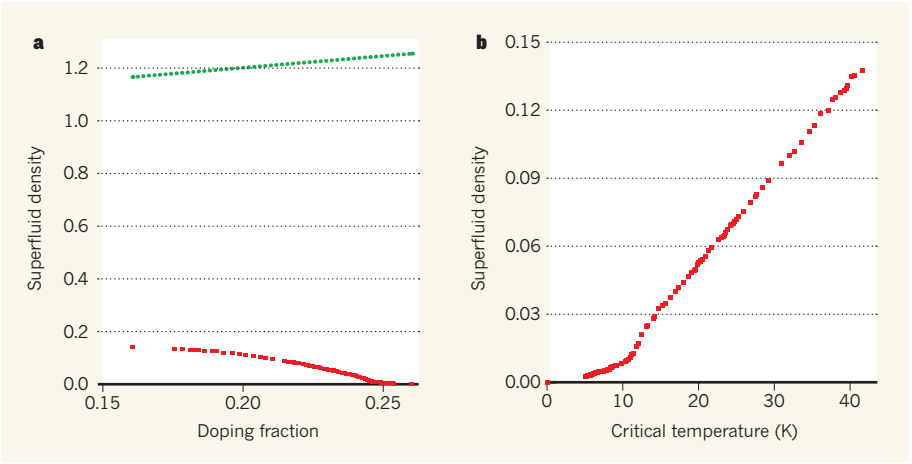

Figure 1 | Surprising superconductivity. Božović *et al.*[5] have measured key properties of 'overdoped' high-temperature copper oxide superconductors. **a**, From their measurements, the authors estimate the superfluid density (red, corresponding to the number of electrons taking part in superconductivity per unit cell; the unit cell is the smallest periodically repeating structure in a crystal) as a function of the doping fraction (a measure of the density of charge carriers). They observe far fewer superconducting electrons than expected from the Bardeen–Cooper–Schrieffer (BCS) theory (green). **b**, The data are presented here as a plot of the superfluid density against the critical temperature (the temperature below which the material can superconduct). The superfluid density is directly proportional to the critical temperature, over a wide doping range. The authors' remarkable results are incompatible with standard BCS theory and require new explanations.

(let's call it Božović's scaling law): the superfluid density is directly proportional to T_c over the entire overdoping range (Fig. 1b). Given the experimental evidence suggesting that BCS theory is at work in this regime[8,9], the findings present a paradox — Božović's scaling law disagrees fundamentally with the predictions of BCS theory, and therefore comes as a complete surprise.

This paradox is partly resolved by a theoretical loophole. Leggett's theorem[10] describes the conditions that must be met for the superfluid density of a system to be equal to the total electron density. One condition is that the system must be translationally invariant — at the atomic scale, the system must be the same at each point in space.

In superconductors, translational invariance does not occur at the atomic scale because the electron system exists in a periodic lattice that is formed from atoms. But in conventional superconductors, quantum physics causes low-energy electronic excitations to behave as though the lattice isn't there. Translational invariance is therefore realized as an emergent symmetry (a symmetry that is seen only on large scales), which means that a BCS superconductor must obey Leggett's theorem.

However, for high-temperature copper oxide superconductors, Božović and colleagues' results suggest that the electron system as a whole remains strongly interacting, even in the overdoped regime. Although such strongly interacting systems are poorly understood, there is experimental evidence that, in the underdoped regime, the superfluid density is not governed by Leggett's theorem[11] because the electrons are greatly affected by the presence of the lattice. Therefore, high-temperature superconductors might not obey Leggett's theorem in the overdoped regime either.

Paradoxes are extremely useful in science: the simple relationship between the superfluid density and T_c suggests that some underlying principle must be at work in overdoped copper oxide superconductors. A similar scaling law has been observed[11] in the underdoped regime, and is explained in terms of electrons binding together in pairs at high temperatures and forming a Bose condensate at T_c. However, this explanation cannot apply in the overdoped regime because of the observed Fermi surfaces. Indeed, there is nothing in the vast literature of superconductivity research that sheds light on this conundrum, and Božović's scaling law forces physicists to go back to the drawing board. ■

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